Organ Printing as a Future Trend of Rapid Prototyping

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Abstract

The shortage of donor organs for patients with diseased organs is an issue which affects every nation. Today, continually advancing science and research has lead to the possible production of artificial organs, and a future vision regarding the permanent and safe implementation of these organs is now a feasible concept. The objective of this essay is to present methods of organ printing. Organ printing is a technique based on the science of tissue engineering and the principles of manufacturing three-dimensional objects using Rapid Prototyping technology. The transplantation of printed organs offers a quick way to extend the quality of life for patients who normally have to accept long waits for donor organs. In addition to the explanation of the historical and theoretical principles of Rapid Prototyping and organ printing, this essay also refers to other possible problems that are addressed by this groundbreaking discovery. Gathered from sources mainly from the fields of medicine and technology, this essay compiles the most significant data to provide insights into the historical background, the current state and future prospects of enabling organ printing outside the body and directly on the human skin.
1 Introduction

A requirement of the Language Award 2010 includes examination and analysis of an arbitrary topic in the field of “Groundbreaking Discoveries in Science and Technology”.

My topic of choice, “Organ Printing as a Future Trend of Rapid Prototyping”, provides a broad overview of the working principles surrounding Rapid Prototyping, and the inceptions of organ printing as a result of enhancements within three-dimensional manufacturing techniques. After outlining the basic concepts of Rapid Prototyping, and presenting possible applications, the importance of organ printing will be explained. I will demonstrate contingent fields of application to depict the expansive potential organ printing might possess, especially within the medical field.

1.1 Relevance of the Topic

In Germany the demand for transplants greatly overweighs the number of available organs. In 2009 about 4,709 transplantations were conducted in Germany, and approximately 12,000 more patients are currently in need of organ transplants.¹ Similarly, in the USA, there are currently about 107,797 people awaiting suitable transplants.² These high numbers express an insufficient supply of organs available for transplantation. By developing a method that enables the rapid production of organs, a groundbreaking discovery in technology and science might address the problem of donor organ shortages. Moreover, the rapid production of organs will benefit the field of product testing, by replacing animal test subjects with artificially manufactured organs.

1.2 Topical Delimitation

This assignment provides basic information about the development of organ printing on the basis of Rapid Prototyping.

Superficially, the working principles of how organs can be printed are examined. Due to the complexity of this subject matter, the topic will be addressed using a simplified explanation of Rapid Prototyping instead of presenting the field of organ printing elaborately.

2 Rapid Prototyping

Rapid Prototyping is a general term for a novel and innovative manufacturing method. This process facilitates the immediate fabrication of work pieces or assemblies using a three-dimensional computer-aided design data file. The first steps towards the development of Rapid Prototyping were carried out in 1987. Today, modern manufacturing methods are based on an application of the work piece in layers.³

2.1 Process of Development

Over the past few years there has been a visible increase of the use of computers. This rise resulted from enhancements within computer-related fields such as CAD (Computer Aided Design) systems. CAD computer software facilitates the design, modification and simulation of three-dimensional parts or assemblies.⁴ Rapid Prototyping is based on CAD technology. The following table presents the historical development of Rapid Prototyping and displays the inception of related technologies.

Table 2.1: historical development of Rapid Prototyping

<table>
<thead>
<tr>
<th>year of development</th>
<th>technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1770</td>
<td>Progress in mechanization</td>
</tr>
<tr>
<td>1946</td>
<td>First computers developed</td>
</tr>
<tr>
<td>1952</td>
<td>First numerical control (NC) machine tool invented</td>
</tr>
<tr>
<td>1961</td>
<td>First commercial robot developed</td>
</tr>
<tr>
<td>1963</td>
<td>Creation of early versions of CAD</td>
</tr>
<tr>
<td>1988</td>
<td>Development of the first commercial Rapid Prototyping system</td>
</tr>
</tbody>
</table>

A prototype usually is a preliminary version of an object, and is often required before the full production of a product can be initiated. The process of Rapid Prototyping involves the following three basic phases. The first phase is called manual or hard prototyping. During this initial phase labor intensive and craft-based techniques are employed rather than traditional methods. The next phase is called soft or virtual prototyping. In this phase, the testing of computer models through CAD has to be completed. The last phase is called rapid prototyping. This third phase implies a solid freeform fabrication. Time efficiency and the possibility to create structurally complex models are the main benefits of this final phase.

2.2 Working Principles

By using a Computer Aided Design/Manufacturing (CAD/CAM) system, a model or component can be designed virtually. This design includes an enclosed volume, and accordingly, closed surfaces are represented. Hereby, the method called surface modeling determines the definition of the surface that has to be filled in order to make the model solid. Therefore, the inside, outside and boundary of the model must be specified by data. By applying solid modeling, the second possibility to create a model, an enclosed volume will be created automatically. The model to be built must now be converted into a special file format which has its source in three-dimensional systems, e.g. “.STL” (STereoLithography). The Rapid Prototyping machine formats this file and creates sliced layers of the model. After the creation of the first layer,

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the model has to be lowered by the next layer. This process continues until the model is complete. Finally, the model and all supports must be removed.\(^7\)\(^8\)

The functional principle of Rapid Prototyping is displayed in the following schematic figure.

![Diagram of Rapid Prototyping](image)

**Figure 2.1: functional principle of Rapid Prototyping\(^9\)**

After the completion of the production process, the working pieces usually have to be reworked manually. The dimensional accuracy amounts to +/- 0.05 mm.\(^10\) Rapid Prototyping working pieces can be used for trial purposes. For example, the process can be applied for manufacturing a prototype before a huge and complex product will be fabricated. Most notably, the use of this method results in time and costs efficiency.\(^11\)

In contrast to the Rapid Prototyping process, the CNC Milling (Computer Numerical Controlled), the traditional method, is a subtractive procedure. From an initial object material is removed until it is in desired

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shape. However, a decisive disadvantage is the low complexity of objects that can be produced with this technique. Especially in the field of medicine, very complicated structures have to be realized physically. This is infeasible with the CNC technology. Despite this disadvantage, the CNC Milling process offers a few advantages over Rapid Prototyping methods. CNC is very precise and allows a very accurate work albeit not very complex structures. Furthermore, many different materials can be used, such as wood, metal, and plastics, whereas Rapid Prototyping procedures are subject to certain materials. Compared to the CNC Milling process, Rapid Prototyping is 50 percent more time efficient and 30 percent more cost efficient.12

The following table presents a selection of common Rapid Prototyping techniques, the working process of each technique, and the appropriate materials used.

<table>
<thead>
<tr>
<th>technique</th>
<th>working process</th>
<th>material</th>
</tr>
</thead>
<tbody>
<tr>
<td>stereolithography (SLA)</td>
<td>primary shaping from the liquid state</td>
<td>epoxy and acrylic resin</td>
</tr>
<tr>
<td>selective laser sintering (SLS)</td>
<td>primary shaping from the granular or powder state</td>
<td>wax, ceramic powder, synthetic granules, metal powder, foundry sand</td>
</tr>
<tr>
<td>laminated object manufacturing (LOM)</td>
<td>primary shaping from material layers in the solid state, contour formation through laser cutting</td>
<td>paper foils, plastic foils, metal foils</td>
</tr>
<tr>
<td>fused deposition modeling (FDM)</td>
<td>primary shaping from the plastic state</td>
<td>thermoplastics, wax wire</td>
</tr>
</tbody>
</table>

In the following, these four methods are listed and explained.

2.2.1 Stereolithography

During this method, a light curable plastic is hardened into thin layers by a laser. The procedure is done in a vat, which is filled with the monomer of the photosensitive resin. After each step, the working piece is lowered a few millimeters into the liquid, and then retracted to a position, which is lower than the layer-thickness of the previous one. A sweeper then distributes the liquid plastic evenly. Then a computer-controlled laser uses movable mirrors and drives over the new layer surface that has to be cured. After the curing process of one layer is completed, the whole procedure will be repeated, so that after many procedures a three-dimensional model emerges.\textsuperscript{14}

\textbf{Figure 2.2: stereolithography}\textsuperscript{15}


2.2.2 Selective Laser Sintering

This is a method to produce spatial structures by sintering powder feedstock. Under high pressure materials are heated to temperatures below their melting temperatures. The working piece is built-up layer by layer. The effect of laser beams may generate any three-dimensional geometry, such as working pieces, which cannot be produced via conventional mechanical or manufacturing fabrications.16

![Selective Laser Sintering Diagram](http://www.custompartnet.com/wu/images/rapid-prototyping/sls.png)

Figure 2.3: selective laser sintering17

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2.2.3 Laminated Object Manufacturing

Here, the mold is mainly constructed of paper layers. Each new layer is laminated onto the existing layer and then the contour is cut using knives, hot wire or laser. Afterwards, the next layers are applied in the same way until the object is finished.\(^{18}\)

\[\text{Figure 2.4: laminated object manufacturing}\]\(^{19}\)


2.3.4 Fused Deposition Modeling

This method is based on the liquefaction of a wire-shaped plastic or wax material by heating. During subsequent cooling, the material hardens again. The application of material is made by extruding a freely movable heating nozzle in the production level. In this way, these single layers merge into a complex part during the production of the model in layers.\textsuperscript{20}

![Figure 2.5: fused deposition modeling\textsuperscript{21}]

2.3 Fields of Application

Through various application possibilities, the industry can benefit from Rapid Prototyping, for example in the fields of automotive, electronics, biomedical engineering, education, aeronautics, life sciences, healthcare and craftwork.

Within a short period of fabrication time, complex physical objects can be used for experiments. With little effect on cost and lead time, parts can quickly be optimized to meet customer and consumer requirements. Furthermore, the method is ideal to avoid errors within tool manufacturing. With a Rapid Prototyping model, it is possible to check fitting accuracy, to test a specific function mechanism or simply to create a model for a fair.22

The following figures display examples of Rapid Prototyping in the field of component parts for electronics and in the field of toys.

Figure 2.6: mobile phone cover23 Figure 2.7: plastics toy24

3 Organ Printing

There are a lot of researchers aimed at investigating how the production of artificial biological tissues and organs might become reality. This field of research is called tissue engineering, an approach that is geared towards meeting donor organ shortages.

Nevertheless, the method does not yet enable the construction of complicated thick tissues. Usually, stem cells are used to create a tissue construct. This means that tissues like skin, cornea or cartilage can grow outside the body and can later be transplanted to a patient. An innovative method in the field of tissue engineering is called bioprinting. The process of bioprinting allows a

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precise arrangement of multiple living cell types and other tissue components into pre-determined sites. Layer-by-layer, a biological structure created by computer-aided design is deposited. This technology works by using modified inkjet printers.\textsuperscript{25, 26, 27}

By pre-forming the material, for example, by computer-assisted design (CAD) based on the data of a three-dimensional computer tomography, three-dimensional custom-made shapes can be created for the reconstruction of skull or jawbone defects. Situation models are made by plastic impression of a defect. Hence, molds are created. Cell-containing gels can then be poured into these molds, so that after polymerization and curing, a three-dimensional part can be built that is exactly adjusted to the defect. A further development of these techniques is Rapid Prototyping. This allows for the computer production of biomaterials, templates or molds by a plotter.\textsuperscript{28}

3.1 Process of Development

The Japanese researcher Makoto Nakamura is one of the pioneers in the new field of organ printing. Instead of microscopic droplets of ink, the printer should hurl thousands of human cells per second out of the print head - and thereby bring them together to build a three-dimensional organ. To prevent the cells from drying out, which can potentially hinder them from merging into a three-dimensional form, they are stored in a solution of sodium alginate and printed on calcium chloride. If a printer places these cells in the right position of the copied organ and repeats this process for all layers, a new three-dimensional organ can be created. Nakamura believes that the first human heart might come out of the printer in approximately 20 years. For patients waiting for a transplant, such a mass production of human organs would be a blessing. A heart from the cells of the patient himself would not cause any rejection by the


immune system. Nakamura began to experiment and noted that drops in the inkjet approximately have the size of human cells: one-hundredth of a millimeter. In 2002, Nakamura bought a commercial printer and tried to equip it with cells. However, the nozzle clogged. After several attempts, the printer company secured support to Nakamura. One year later, the first breakthrough could be noted: Nakamura was able to print cells that survived the printing process. Nakamura was one of the first researchers who produced a three-dimensional structure of real living cells using an inkjet printer. In the future this technology could pave the way for the use of stem cells – and thus for the creation of healthy organs.29

3.2 Working Principles

Biological tissues are characterized by a microscopic structure, a composition containing various components such as multiple kinds of cells and proteins, and a three-dimensional structure. To enable the precise positioning of multiple types of cells onto intended spatial locations in three dimensions, a bioprinting machine applying color inkjet, laminating printing, and precision technologies has to be designed. As mentioned before, Nakamura discovered that common inkjet printers are capable of precisely ejecting small amounts of ink droplets onto accordant positions at a speed of a few ten thousand droplets per second. The resolution resembles the one of individual cells. Since bioprinting deals with living cells and raw biomaterials, it has to be noted that these naturally differ from conventional printing inks. The influence of inkjet printing on living cells and bioactive proteins has to be examined to identify appropriate printing methods and gather a method of building three-dimensional structures with biological materials. The challenge is to procure three-dimensional digital data for native organs from histological specimens and design appropriate artificial tissues. Hereby, the objective is to use those data and the developed bioprinting machine to produce living tissues.30

For the printing process a special ink is used. The name bioink derives from fusion upon contact during the post-printing structure forming operation. To develop the bioink, living cells first have to be spun in a centrifuge, then chopped and then tumbled. The outcome of this process are tiny balls featuring the consistency of a fluid. These balls have to be loaded into a syringe-like nozzle on the printer and extruded out. The structuring process involves the arrangement of the multicellular droplets into a ring. After each ring, the printer extrudes a thin layer of gel to fake a matrix that surrounds cells in living tissue. These steps have to be repeated until the creation of the structure is completed. The layers of gel later relax and the rings merge into a smooth cylinder. Such hydrogels, also called biopaper, guarantee a rapid solidification of the structure during and after the printing process. Hydrogels are used to mimic the natural cell environment. Various hydrogel components are blended as liquids, a gel is built and within a short period of time biopaper is formed by self-assembly through crosslinking. Different cells require different hydrogels depending on the desired structure. Besides the head that extrudes the bioink, a second head of the printer deposits the biopaper scaffold that supports the cellular droplets without interfering with them. The hydrogel construct allows the cellular droplets to merge together. After the completed fusion process, the biopaper can be removed.

Researchers are currently working on discovering precise patterns of cells required for each organ to create organs.  

The following schematic illustration shall depict the working process of bioprinting a tubular organ module. A machine resembling a common inkjet printer is applied to print out living structures.

Figure 3.1: bioprinting on demand

The organ printing method implies three main steps:
1) Preprocessing or computer-aided design of organs
2) Processing of an actual printing and fast solidification of the organ constructs
3) Postprocessing

**Preprocessing**
First, a blueprint must be developed before the building can be initiated. This blueprint is composed via a computer-aided design of the projected organ that offers spatial information about the placement of the cells in the three-dimensional organ on the basis of histological structure. Through techniques like clinical bioimaging and ultrasound it is possible to gain sophisticated information regarding anatomical characteristics of organs without even extracting them from the human body.

**Processing**
Actual printing of organ constructs will be physically accomplished by inkjet printers because they operate at a very fast speed. An automatic robot deposition device facilitates a precise application of the biological material. This device is composed of a syringe combined with a robotic hand. It shall be noted that this is a very expensive technique. Despite the feasibility of organ printing, there are still challenges that have to be faced and problems to be met. An effective vascularization of printed organs is as important as to maintain the shape of three-dimensional tissue constructs to prevent the printed organs from melting and deforming.

**Postprocessing**
After the printing process is completed, the organ structures are not functional organs, yet. Thus, they have to undergo certain self-assembly, maturation and differentiation procedures. The tissues have to strive for a state of an elastic solid. The process of becoming such a solid organ is called accelerated tissue maturation. Furthermore, viable printed organs require a watery environment. To achieve this, a bioreactor – a special perfusion device – is used to secure the survival of the cells. Although it is not proven, yet, if the bioreactor shall be part of the bioprinter, it might be beneficial to place it in a separate environment regarding costs and engineering. Hence, the bioprinter could operate rather productively while printed organs can be placed separately for
postprocessing. Moreover, various chemical and mechanical requirements of each organ have to be considered.\textsuperscript{36}

The following picture illustrates a bioreactor used to maintain the viability of the tissue, to monitor the maturation process, to store the tissue and to enable transportation.

![Figure 3.2: perfusion minibioreactor\textsuperscript{37}]

3.3 Fields of Application

This essay concentrates on the use of organ printing in the field of human medicine for transplantation of organs. By means of organ printing, waiting times for organs could be shortened drastically, and thus save many lives. However, it is not always the breeding of transplantable organs that is essential. For scientists, breeding human organs would also be extremely useful to test the effects of drugs and other new procedures. Typically, new drugs are often tested first on animals. Nevertheless, the results are only rarely transferable to humans. Even more rarely, effective therapies can be developed from those results. Thus, rapid cultured human organs could enable more effective drug testing.\textsuperscript{38}

The following computer-simulated illustration presents a printed human part.

![Figure 3.3: printed organ](http://www.mis-asia.com/__data/assets/image/0004/170239/Organ-printer_ed.jpg) [Accessed 1 September 2010].

4 Future Prospects

Through clinical experience it could be proven that organ transplantation in cases of a patient’s deteriorated organ can save the person’s life. Due to a shortage of donor organs, patients in need of healthy organs have to accept long waiting periods. To ensure the supply of organs, and to face problems of aging, organ printing might offer a momentous remedy that could potentially extend people’s lives.40

The US company Organovo specializes in regenerative medicine. In December 2009, they made public that they acquired a new $200,000 bioprinter to print artificial organs making use of inkjet technology. The Australian partner engineering firm Invetech designed the world’s first fully functional three-dimensional bioprinter. After this announcement, Invetech claimed to ship even more bioprinters to Organovo in 2010 and 2011 to support research on bioprinting. Organovo’s Scientific Founder and Chief Scientific Officer, Dr. Gabor Forgacs, anticipates that organ printing using a

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patient’s own cells will be feasible one day. Using patient’s own cells guarantees that the recipient will not reject the new transplanted organ. Stem cells can convert into other cell types. Depending on the types of stem cells, they have the potential to differentiate into any tissue or into certain specified types of tissues. However, printed organs might not exactly appear like real organs, but they would be fully functional.

In 1999, Dr. Anthony Atala, M.D. and his colleagues at the Wake Forest Institute for Regenerative Medicine in North Carolina were even growing artificial bladders successfully used in human trials. Now, Wake Forest scientists are engaged in growing more than 22 different types of organs and tissues. Among the objectives is the vision to manufacture bioprinters that are capable of printing tissues and organs into a body. At the moment, Dr. Atala is concentrating on the development of a bioprinter that scans the contours of a body part that is longing for a skin transplant, and then prints skin directly onto it. Organovo’s Dr. Forgacs even intends to produce these organs in various shapes and sizes, so to say customized designer organs.41

The idea is tempting, but the implementation will definitely still cause great difficulties for years to come. Among other things, the artificial organs have to function for decades. There are stem cells that can – provided with appropriate additions – transform into all kinds of tissue types. Nevertheless, the researchers still face several obstacles: Stem cells are in limited supply, and required ingredients for a particular tissue type is in most cases unknown. An incorrect or improper dosed substance can have severe consequences such as cancer, for instance. Moreover, the human body could reject a bioartificial organ one day because it is identified as a foreign part, similar to that reaction to a donor organ.42

5 Conclusion

Due to the complexity of the issue in this essay, basic information for easy comprehension is reproduced without extensive explanations in detail. This mainly includes the development of the Rapid Prototyping technology, its working principles and the ensuing operation of organ printing.

I consider this method as a groundbreaking discovery in science and technology, especially in the medical field because life-saving artificial organs could be transplanted into patients, who would have to wait very long for a donor organ. Moreover, donor organs harbor the risk that the body identifies this organ as foreign what might result in a rejection. By using patients' own cells in the organ printing process, this reaction would be counteracted. Although the production of artificial organs and the process itself by using bioprinters sound simple and are explained in detail in literature, the actual implementation is difficult for me to grasp and to imagine, but also very fascinating. Thus, I am looking forward to the future developments in research in the field of organ printing. Particularly, it will be of interest, if there will be a mass production of organs printed by bioprinters one day that may save and extend many lives. Finally, rapid printed organs could hopefully provide enough organs to secure humans, and to terminate animal experiments.
References


